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Dedicated to B.I. Buzykin on His 80th Anniversary

Synthesis and Antioxidant Activity of Sterically Hindered Phenol Derivatives of Carboxy- and Sulfobetaines

R. G. Tagasheva[a]*, E. R. Shakirova[a], S. V. Bukharov[a], I. V. Galkina[b], G. K. Ziyatdinova[b], R. Z. Musin[c], and I. Kh. Rizvanov[c]

[a] *Kazan National Research Technological University, ul. K. Marksa 68, Kazan, Tatarstan, 420015 Russia*
**e-mail: roza-ta1982@yandex.ru*

[b] *Kazan (Volga Region) Federal University, Kazan, Tatarstan, Russia*

[c] *A.E. Arbuzov Institute of Organic and Physical Chemistry, Kazan Scientific Center, Kazan, Tatarstan, Russia*

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Abstract—New multifunctional antioxidants based on carboxy- and sulfobetaines with sterically hindered phenol fragments were synthesized. The antioxidant capacity of the compounds determined in the reactions of their oxidation by electrogenerated bromine is comparable to that of ascorbic acid and ionol.

Keywords: antioxidants, betaines, sterically hindered phenols, antioxidant capacity

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Betaines have various practically useful properties. Among them, effective antidiabetic and cardioprotective medicines, as well as compounds possessing bactericidal and disinfecting properties, were found. They are widely used as the components of cosmetics for skin and hair care and in children's cosmetics. Some betaines can enhance the antioxidant effect of vitamins C and E as well as transport the biologically active substances through the mitochondria membranes [1].

Phenol antioxidants possess a wide spectrum of biological activity based primarily on the ability to correct oxidative stress [2]. At the same time much attention is paid to their targeted delivery to mitochondria – cells' energy "factories" in which oxidation-reduction processes take place most actively and the concentration of active forms of oxygen is the highest [3].

Here we report on the synthesis of sterically hindered phenol derivatives of some carboxy- and sulfobetaines.

In the first step, the corresponding amidoamines **4a**, **4b** and bis-amines **5a**, **5b** were prepared by the reaction of bis-amines **1a**, **1b** with methyl 3,5-di-*tert*-butyl-4-hydroxyphenylpropionate **2** and 3,5-di-*tert*-butyl-4-hydroxybenzyl acetate **3** (Scheme 1). The synthesis of compounds **4b** and **5b** has been previously described in [4]. Due to the reversibility of the conversion and the low reactivity of bis-amines **1a**, **1b** with respect to ester **2**, the reactions were carried out with use of an excess of compounds **1a**, **1b** with prolonged heating and distillation of methanol. Benzyl acetate **3** readily reacted with bis-amines **1a**, **1b** at room temperature (Scheme 1).

Carboxy- and sulfobetaines were obtained by reactions of amidoamines **4a**, **4b** with sodium chloroacetate, 1,3-propanesultone and sodium 3-chloro-2-hydroxypropylsulfonate (Scheme 2).

For amides, hydrazides, and acylhydrazones *cis*/*trans* isomerism is characteristic due to the hindered rotation in the NC(O) fragment [5]. Apparently, the presence of such a hindered rotation causes some nonequivalence of the geminal protons of the methylene groups and their manifestation in the ^{1}H NMR spectra of **4a**, **4b** and **6**–**8** in the form of more complex multiplets compared to the expected triplets.

In spite of the presence of two tertiary amine groups in bis-amines **5a**, **5b** their reactions with 1,3-